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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,372	09/22/2003	Isabelle Nonotte	016800-643	5014

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,372	NONOTTE ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,9,10,13-15,17,18,21,45-48,50-53,55-59,61,68 and 69* is/are pending in the application.

4a) Of the above claim(s) *5, 38-39, 41-42, 44, 49, 62-65, 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,9,10,13-15,17,18,21,45-48,50-53,55-59,61,68 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of, Amendments/Remarks filed 9/5/06 is acknowledged. Claims **1-2, 6-7, 9-10, 13-15, 17-18, 21, 45-48, 50-53, 55-59, 61, 68-69** are pending in this application. Claims 5, 38-39, 41-42, 44, 49, 62-65, 67 are withdrawn as being directed to a non-elected invention. Claims 3-4, 8, 11-12, 16, 19-20, 22-37, 40, 43, 54, 60, 66 stand cancelled.

Information Disclosure Statement

Applicant states that JP 403017004 has been resubmitted and attached an IDS for consideration. However, the record indicates that applicant has not filed an IDS or re-submitted JP '004 for the examiner to consider.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48, 56-59, 61, and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 is directed to a method of combating skin pallor comprising administering an effective amount of manganese and a bioaffecting amount of at least one member from the group consisting of alverine, alverine salts, keratolytic agent, chlorine-channel openers, hydroxy acids, and retinoids, *wherein manganese is the sole ingredient for treating skin pallor*. The claim is vague and indefinite since the claim has two contradictory limitations. For instance, the claim requires that only manganese is the sole active agent for combating skin pallor; however

keratolytic agents such as salicylic acids have the capability of also combating skin pallor. Therefore, the metes and bounds of the claim are unclear.

Claim 56 has been amended to a method of combating skin pallor comprising topically administering an effective amount of manganese selected from organic salts of manganese and manganese-rich microorganism and a bioaffecting amount of at least one member from the group consisting of alverine, alverine salts, keratolytic agent, chlorine-channel openers, hydroxy acids, and retinoids, *wherein manganese is the sole ingredient for treating skin pallor.* As pointed out above, the claim is vague and indefinite since the claim has two contradictory limitations. For instance, the claim requires that only manganese is the sole active agent for combating skin pallor; however keratolytic agents such as salicylic acids have the capability of also combating skin pallor. Therefore, the metes and bounds of the claim are unclear.

Response to Arguments

Applicant argues that the claims have been amended to remove alverine its salts and chlorine channel openers and thus it overcomes the rejection.

Applicant's arguments filed 9/5/06 have been fully considered but they are not persuasive. The examiner points out that amended claim 48 still recites a bioaffecting amount of keratolytic agent, retinoids, hydroxyl acids, which is indefinite since as pointed out in the rejection, keratolytic agents also have the capability of combating skin pallor. Applicant has not addressed this.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-2, 9, 13, 17, 21, 47, 52, and 55 under 35 U.S.C. 102(b) as being anticipated by JP 04108710 to Shiga (abstract only) is withdrawn in view of the amendments of 9/5/06 limiting the claims to manganese organic salts or manganese-rich microorganism.

The rejection of claims 1-2, 6-7, 13-15, 21, 47, 50-51, and 55 under 35 U.S.C. 102(e) as being anticipated by Pauly (6,274,123) limiting the claims to manganese organic salts or manganese-rich microorganism.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 6-7, 9-10, 13-15, 17-18, 21, 45-48, 50-53, 55-59, 61, and 68-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breton et al (5,900,257) by itself or in further view of Questions and Answers About Raynaud's Phenomenon distributed by the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Breton teaches a cosmetic, dermatological or pharmaceutical compositions comprising at least one lanthanide, manganese, tin or yttrium salt as a substance P antagonist for the treatment of disorders associated with an excessive synthesis and/or release of substance P and for the treatment of sensitive skins. See abstract. Breton teaches substance P is involved in the

transmission of pain and in diseases of the central nervous system including skin disorders and vasospastic disorders (for example, migraine, Raynaud's disease). See column 1, lines 35-60 and especially lines 54-55.

Breton teaches the at least one lanthanide, manganese, tin or yttrium salt is formulated into a cosmetic or dermatological or pharmaceutical composition for the treatment of disorders of the central nervous system, allergic syndromes, inflammation, pain, gastrointestinal disorders, skin disorders, fibrosis, collagen maturation disorders, cardiovascular disorders, vasospastic disorders, immunological disorders, as well as disorders of the urinogenital tract, ophthalmic and pancreatic disorders. See column 2, lines 35-50.

In the field of skin or cutaneous disorders, Breton teaches it is known that certain skins are more sensitive than others. Breton teaches sensitive skins could be divided into two main clinical forms, irritable and/or reactive skins and intolerant skins. An irritable and/or reactive skin is a skin which reacts through itching or through pricking in reaction to various factors including the environment, *emotion*, food, the wind, rubbing, shaving, soap, surfactants, hard water with a high concentration of calcium, *temperature variations* or wool. An intolerant skin is a skin which reacts, through sensations of warming inflammation, stabbing pain, pins and needles and/or reddening, to various factors such as the environment, emotions, etc. See column 3.

The lanthanide, manganese, tin, or yttrium salt are formulated in an amount ranging 10^{-5} to 20%, preferably from 0.5% to 8% of the total weight of the composition and the salts form may be selected from carbonates, bicarbonates, sulfates, glycerophosphates, borates, chlorides, nitrates, acetates, hydroxides, and persulfates. See column 4, lines 40-65.

Breton teaches for topical application the composition is formulated into emulsions, liquids, gels, creams, etc. See column 5, lines 1-15. Additional active agents that are utilized in the composition include keratolytic agents, i.e. hydroxy acids (glycolic acid, lactic acid, salicylic acid, citric acid, fruit acids, and n-octanoyl-5-salicylic acid). See column 7, lines 15-25. Breton discloses that exemplary active agents include hydroxyl acid. See column 7, lines 65-67.

Specifically example 3 teaches a care cream comprising 15% manganese chloride, 2% glycerol (physiologically acceptable alcohol), methyl paraben (preservative), perfume, and water.

Breton does not exemplify the method of treating vasospastic disorders.

Although Breton does not specify treating vasospastic disorders including Raynaud's phenomenon, it is would have bee obvious for a skilled artisan at the time the invention was made to look to the guidance provided by Breton and utilize the manganese formulation to treat a vasospastic disorder which would in turn treat skin pallor. One would be motivated to do so since Breton teaches salts including manganese are utilized in treating disorders wherein substance P is involved since the salts (manganese) act as substance P antagonists and thus the salts may be used to treat vasospastic disorders. Vasospastic disorders are characterized as the persistent contraction of blood vessels, which reduces blood flow in the vessels. Therefore, if a skilled artisan treated a vasospastic disorder by increasing the blood flow utilizing the substance P antagonist, then is obvious skin pallor will be treated since skin pallor is caused by the lack of blood circulation.

Furthermore, it is would have bee obvious for a skilled artisan at the time the invention was made to combine the teaching of Breton and the pamphlet on Raynaud's Phenomenon and

expect to treat skin pallor (skin pallor caused by stress) by utilizing Breton's composition comprising manganese. The pamphlet teaches Raynaud's Phenomenon is a vasospastic disorder which is characterized by episodic attacks called vasospastic attacks that cause the blood vessels to constrict and during the attack the skin changes color from pallor wherein the skin turns white due to the lack of blood flow. Further, the pamphlet discloses stress, temperature, and emotional upsets trigger the attacks. Therefore, a skilled artisan would have expected to treat skin pallor by utilizing Breton's manganese composition since firstly Breton suggests the use of the manganese composition to treat vasospastic disorders such as Raynaud's Phenomenon and secondly the pamphlet on Raynaud's Phenomenon states that Raynaud's is a vasospastic disorder that is characterized by skin pallor and triggered by emotional or physical stress.

Response to Arguments

Applicant argues that independent claims 1, 2, 47, and 48 are directed to a method of combating skin pallor by administering a composition including a manganese organic salt or manganese-rich microorganism extract, which is used in a skin pallor reducing amount. Applicant argues Breton does not discloses or fairly suggest an effective skin pallor reducing amount of the instant manganese forms. Further, applicant argues that the instant claims are directed to topical administration and Breton does not teach this. Applicant argues that the NIAMSD article does not overcome these deficiencies. Applicant argues NIAMSD does not discloses or fairly suggest an effective skin pallor reducing amount of the instant manganese forms. Applicant argues the examiner has not considered all the words.

Applicant's arguments filed 9/5/06 have been fully considered but they are not persuasive. The examiner points out that "all the words" and limitations have been full

consideration. Firstly, as discussed in the above rejection Breton teaches administering a substance P antagonist including a salt of yttrium, lanthanum, cerium, praseodymium, neodymium, promethium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, thulium, ytterbium, lutetium, tin, manganesė to treat skin disorders and vasospastic disorders (for example, migraine, Raynaud's disease). See column 1, lines 35-60 and especially lines 54-55. Specifically, a manganese salt is taught in example 3. As explained in the above rejection, vasospastic disorders are characterized as the persistent contraction of blood vessels, which reduces blood flow in the vessels. Thus, if a skilled artisan treated a vasospastic disorder by increasing the blood flow utilizing the substance P antagonist, then skin pallor will obviously be treated since skin pallor is caused by the lack of blood circulation. With regard to the limitation "resulting from stress", it should be noted that claiming the cause of skin pallor does not impute a patentable distinction unless skin paleness caused by stress specifically imparts a different characteristic than other skin paleness caused by other sources. Moreover, the examiner points out that the NIAMSD article clearly teaches that in Raynaud's Phenomenon, a vasospastic disorder taught by Breton, is characterized by episodic attacks that cause the blood vessels to constrict and during the attack the skin changes to a white color due to the lack of blood flow and this attack is triggered by *stress, temperature, and emotional upsets*. Thus, clearly the combination of Breton alone or in combination with NIAMSD teaches the instant methodology and the treatment of the specified population.

Secondly, the examiner points out that Breton teaches the substance P antagonist may be administered topically on column 5, lines 5-20.

> For **topical** application onto the skin, the composition may have the form, especially, of an aqueous, aqueous-alcoholic or oily solution, or of an oily suspension, or of a dispersion of the lotion or serum type, of emulsions of liquid or semi-liquid consistency of the milk type, which are obtained by dispersing a fatty

> phase in an aqueous phase (O/W) or, conversely, (W/O), or of suspensions or emulsions of soft consistency of the cream type or of aqueous or anhydrous gels, of micro-emulsions or, alternatively, microcapsules or microparticles, or of vesicular dispersions of the ionic and/or nonionic type. These compositions are formulated via the usual techniques

Moreover, example 3 teaches a manganese chloride care lotion.

Thirdly, Breton teaches the instant organic salts of manganese on column 4, lines 40-65.

> Exemplary such salts include carbonates, bicarbonates, sulfates, glycerophosphates, borates, chlorides, nitrates, acetates, hydroxides, persulfates as well as salts of. alpha.-hydroxy acids (citrates, tartrates, lactates, malates) or of the fruit acids in general, or, alternatively, salts of amino acids (aspartate, arginate, glycocholate, fumarate) or salts of fatty acids (palmitate, oleate, caseinate, behenate).

The examiner points out that although Breton only exemplifies manganese chloride, clearly other salts including the instant organic salts are taught. The examiner points out that disclosed examples and preferred embodiments do not constitute a teaching away form the broader disclosure or nonpreferred embodiment". In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Thus, it is within the skill of an artisan to substitute one salt for another absent the unexpectedness of the instant salts, as taught by Breton.

With regard to the instant effective amount, it is noted that on page 7 of the instant specification, applicant discloses that to manganese is administered in an amount of 0.0001-10%. The examiner points to column 4, lines 60-65 wherein Breton teaches:

> According to the present invention, the salt is advantageously formulated in an amount ranging from 10.sup.-5 % to 20% of the total weight of the composition and, preferably, in an amount ranging from 10.sup.-2 % to 15% of the total weight of the composition and, more preferably, from 0.5% to 8% of the total weight of the composition.

Again the examiner points out that although example 3 utilizing 15% of the manganese salt, this does not teach away from the broader range of 10.sup.-5 % to 20%, preferably 10.sup.5% to 15%, and most preferably 0.5-8%. The instant claimed range of 0.0001-1% in independent claims 6, 14, 50, and 56 falls within the prior art's range of 10.sup.5% to 15% and

0.5-8%. Applicant has not provided any unexpectedness of this specific range and thus it is the examiner's position that the claimed range in obvious over the prior art.

With regard to the instant claim language, although independent claims 1-2, 6, and 14 recite "consisting" language, the examiner points out that the claims also recites water and at least one member from the group selected from alcohols, oils, fatty acids, waxes, emulsifiers, gelling agents, preservatives, fillers, colorants, fragrances, etc. Thus, the instant claim language is not limiting. The examiner specifically relies on example 3 of US '257. The composition comprises 15% manganese chloride (active), 2% glycerol (physiologically acceptable alcohol), methyl paraben (preservative), perfume (fragrance), and water.

Lastly, Breton teaches the claimed excipients and bioaffecting agent, specifically keratolytic agents on column 7, lines 65-67.

Thus, clearly all the claim limitations have been given full consideration.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Examiner
Art Unit 1616